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Can Colchicine as an Old Anti-Inflammatory Agent Be Effective in COVID-19?

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A pneumonia of unknown source was first reported to the World Health Organization Country Office from Wuhan, China, on December 31, 2019. Analysis of the samples obtained from the lower respiratory tract confirmed a novel coronavirus, which is now known as coronavirus disease 2019 (COVID-19). On March 11, 2020, the World Health Organization stated that COVID-19 was a pandemic disease with a mortality rate of about 3.7%.[1,2] Recently, several studies have reported that a subgroup of patients with intense COVID-19 could have suffered from a cytokine release syndrome (CRS).[2] CRS is a potentially life-threatening toxicity with an initial increase of tumor necrosis factor-α (TNF-α), followed by an increase in interleukin (IL)-1β, IL-2, IL-6, IL-8, IL-10, and interferon-γ (IFN-γ).[3] A cytokine profile was detected in COVID-19, including increased IL-2, IL-7, IFN-γ, granulocyte colony-stimulating factor, monocyte chemoattractant protein 1, macrophage inflammatory protein 1-α, and TNF-α.[4] In addition, increased ferritin and IL-6 were introduced as predictors of fatality in COVID-19.[5] All reported data could be considered as proof, confirming the activation of inflammation processes and the occurrence of CRS in critical patients with COVID-19.

Colchicine is as an old drug, an alkaloid derived from autumn crocus, which has been used to treat several inflammatory diseases for many years. Several mechanisms of action for the anti-inflammatory effects of colchicine have been reported in the literature.[6,7] The ability of colchicine to bind to free tubulin dimers, which may result in the blockage of the following microtubule polymerization,[8] is believed to be one of the most famous mechanisms. This mechanism seems to lead to the interruption of inflammatory cell activities and cytokine release.[9] Moreover, colchicine may control the white blood cell (WBC)-mediated inflammatory activities, counting the inhibiting WBC production of superoxides and release of numerous cytokines and pyrogens.[10] Therefore, it may generally target WBCs, resulting in microtubule depolymerization, which in turn inhibits motility, phagocytosis, and degranulation of the WBCs. Furthermore, colchicine may suppress IL-1β and IL-18 release by interacting with Nod-like receptor protein 3 inflammasome protein complex.[11]

Colchicine is approved for the treatment of patients with acute gout and familial Mediterranean fever as well as other inflammatory conditions, including pericarditis and acute coronary syndrome (ACS), urarthritis, and other disorders.[12-14]

Martínez et al[13] studied the effect of colchicine on local cardiac production of inflammatory cytokines in patients with ACS. They concluded that the local cardiac production of inflammatory cytokines containing IL-1β, IL-18, and IL-6 were elevated in patients with ACS. It was also inferred that the treatment with short-term colchicine could quickly and predominantly decrease the levels of IL-1β, IL-18, and IL-6 cytokines.

Recently, Mehta et al[2] recommended that immunosuppression could be useful in patients with severe COVID-19 by hyperinflammation.

According to a recent hypothesis, production of the inflammatory cytokines such as IL-1β and IL-6 is a key downstream inflammatory mechanism in patients with severe COVID-19. Therefore, colchicine, as a simple and cheap drug with adequate safety profile, can be

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proposed as a potential candidate for alleviating the inflammatory conditions. However, to the best of our knowledge, only a phase 3, multicenter, randomized, double-blind, placebo-controlled multicenter study has been recently assigned to clinicaltrials.gov by Montreal Heart Institute, to investigate the efficacy and safety of colchicine in adult patients diagnosed with COVID-19 with a minimum of 1 high-risk criterion (NCT04322682). In addition, we have designed a study to evaluate the efficacy and safety of a combination of colchicine and TNF-α inhibitors in patients with severe COVID-19. This combination was selected based on the mentioned potential therapeutic effects of colchicine and TNF-α inhibitors due to possible effects in modulation of severe acute respiratory syndrome coronavirus infection.[15]

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Conflicts of Interest

The authors declare no conflicts of interest.

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Author Contributions

All authors performed the literature search, wrote the manuscript, and approved the final manuscript.

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